I. Amendments to the Specification:

On page 1, please delete the heading "Related Applications" and the first full paragraph and insert the following heading and paragraph in amended form:

CROSS-REFERENCE TO RELATED APPLICATIONS

The present application is a division of U.S. Patent Application No. 09/353,368, filed July 14, 1999, which claims benefit of Provisional Application Serial No. 60/134,839, filed May 19, 1999, and benefit of U.S. Patent Application No. 09/115, 667, filed July 14, 1998 (since converted to Provisional Application No. 60/150,690). The present application is related to U.S. Patent Application Nos. 09/574,110 and 10/631,883. The disclosures of each of the foregoing are hereby incorporated by reference in their entirety.

On page 5, please delete the first full paragraph, lines 13-20, and insert the following in amended form:

Related members of the vancomycin class of glycopeptide antibiotics include the ristocetins, the eremomycins, the avoparcins and teicoplanin. Several of these compounds are shown, together with vancomycin in Figures 1a and 1b. The chemical structures of all of these compounds include a dalbaheptide structure as the aglycone core, with minor differences in the amino acids and in the cross-linking, but differ from each other most distinctively in terms of the nature of the sugar residues as well as the number and points of attachment of sugar residues to the aglycone core. It is known that biological activities of vancomycin-type antibiotics vary depending on the nature of the sugar residues.

On page 8, please delete the second full paragraph (the first paragraph following the heading SUMMARY OF THE INVENTION), and insert the following paragraph in amended form:

This invention is directed to glycopeptide compositions which have the formula A_1-A_2-A_3-A_4-A_5-A_6-A_7, SEQ ID NO:1 in which each dash represents a covalent bond; wherein the group A_1 comprises a modified or unmodified α-amino acid residue, alkyl, aryl, aralkyl, alkanoyl, aroyl, aralkanoyl, heterocyclic, heterocyclic-carbonyl, heterocyclic-alkyl, heterocyclic-alkyl-carbonyl, alkylsulfonyl, arylsulfonyl, guanidinyl, carbamoyl, or xanthyl;

residue, whereby (i) the group A_1 is linked to an amino group on the group A2, (ii) each of the groups A_2, A_4, and A_6 bears an aromatic side chain, which aromatic side chains are cross-linked together by two or more covalent bonds, and (iii) the group A_7 bears a terminal carboxyl, ester, amide, or N-substituted amide group.

On page 11, please delete the first full paragraph and insert the following in amended form:

Figure 1a contains structure diagrams of vancomycin and related glycopeptide antibiotics.

Figure 1b contains structure diagrams of vancomycin-related glycopeptide antibiotics.

On page 11, please delete paragraphs eight, nine and ten and insert the following in amended form:

Figure 8a illustrates further functionalization of a glucose C6 amino substituent on vancomycin.

Figure 8b illustrates further functionalization of a glucose C6 amino substituent on vancomycin.

Figure 9a illustrates substitution of [[both]] the glucose C6 position ~~and the vancosamine nirogen~~.

Figure 9b further illustrates substitution of the vancosamine nitrogen.

Figure 10a illustrates introduction of a thio substituent[[s]] at the glucose C6 position of vancomycin.

Figure 10b illustrates introduction of a thio substituent at the glucose C6 position of vancomycin.

On page 12, please delete the first paragraph and insert the following in amended form:

Figure 11a illustrates removal of the A_1 amino acid of vancomycin and protection of the product ~~to allow reaction at the A_2 terminal amino group~~.

Figure 11b illustrates the protected product formed from the removal of the A_1 amino acid of vancomycin and a reaction at the A_2 terminal amino group.

The glycopeptide compositions of this invention have the formula formula A_1-A_2-A_3-A_4-A_5-A_6-A_7, <u>SEQ ID NO:1</u> in which each dash represents a covalent bond; wherein the group A_1 comprises a modified or unmodified α-amino acid residue, alkyl, aryl, aralkyl, alkanoyl, aroyl, aralkanoyl, heterocyclic, heterocyclic-carbonyl, heterocyclic-alkyl, heterocyclic-alkyl-carbonyl, alkylsulfonyl, arylsulfonyl, guanidinyl, carbamoyl, or xanthyl; wherein each of the groups A_2 to A_7 comprises a modified or unmodified α-amino acid residue, whereby (i) the group A_1 is linked to an amino group on the group A2, (ii) each of the groups A_2, A_4, and A_6 bears an aromatic side chain, which aromatic side chains are cross-linked together by two or more covalent bonds, and (iii) the group A_7 bears a terminal carboxyl, ester, amide, or N-substituted amide group.

On page 17, please delete the last full paragraph, (lines 18-29), and insert the following in amended form:

Preferably, residues A_2 to A_7 of the glycopeptide are linked sequentially by peptide bonds and are cross-linked as in a dalbaheptide, as defined hereinabove. The preferred glycopeptides thus have a peptide core in which the residues are linked as in the natural glycopeptide antibiotics, as shown in Figure<u>s</u> 1<u>a and 1b</u>. Substitution of different amino acids at A_3 is permitted, as are modified amino acid residues at all positions, as described hereinabove. In a preferred embodiment of this invention, residue A_1 is an α-amino acid. which may be substituted on the terminal amino group by alkyl, aryl, aralkyl, alkanoyl, aroyl, aralkanoyl, heterocyclic, heterocyclic-carbonyl, heterocyclic alkyl, alkylsulfonyl, arylsulfonyl, guanidinyl, carbamoyl, or xanthyl, and the structures and interconnections of A_1 to A_7 are those of vancomycin, i.e., the glycopeptide has the heptapeptide core of vancomycin, subject to the amino acid modifications and substitutions on A_1 to A_7 described hereinabove.

On pages 20-21, please delete the only paragraph on page 20 and the first paragraph on page 21 and insert the following in amended form:

Protection of both amines by a similar group requires using excess acylation reagent while selective protection of the *N*-methyl leucine residue is known, allowing selective functionalization of the vancosamine amine group. See Pavlov et al., J. Antibiotics, 1993, 46,

displacement of primary arylsulfonyl groups directly, or by further synthetic modification of initial displacement products, including azido and iodo groups. For example, the iodo group is displaced by a variety of nucleophiles to produce additional C6-derivatives. A preferred nucleophile is a thiol compound, especially a heterocyclic thiol. Modification of an azido group at the 6-position is performed, e.g., by reducing the azido group to an amino group, which in turn is functionalized by means of reductive alkylation, nucleophilic substitution, or other amino-group reactions well known to those skilled in the art. These approaches are illustrated in Figures [[7-10]] 7, 8a, 8b, 9a, 9b, 10a and 10b, and in many of the Examples. In a preferred embodiment of the invention, an azido group is partially reduced by reaction with a phosphine compound to produce an iminophosphorane.

On pages 26-27, please delete the last paragraph (lines 28-31 on page 26) and the first paragraph (lines 1-11 on page 27) and insert the following in amended form:
An alternative method for construction of a library of glycopeptide compounds starts with the synthesis of a suitably protected pseudoaglycone. A protected glycopeptide antibiotic having a disaccharide at residue A_4, i.e., a pseudoaglycone bearing an additional sugar residue, is treated with a Lewis acid in an organic solvent to remove the additional sugar residue, as illustrated in Figures 15a and 15b, and in the Examples. In a preferred embodiment of the invention, the Lewis acid is boron trifluoride, preferably as the complex with diethyl ether. When the glycopeptide antibiotic is vancomycin, it is preferred that allyloxycarbonyl (aloc) groups are present on the amines of A_1 and the vancosamine residue, acetates on the aliphatic hydroxyl groups, allyl phenyl ethers on the phenolic hydroxyls, and an allyl or o-nitrobenzyl ester on the A_7 terminal carboxyl; when solid-phase synthesis is employed, the o-nitrobenzyl ester is preferred. A degradation reaction proceeds which removes the additional sugar residue, leaving a pseudoaglycone in which all reactive functional groups (amine, carboxylic acid, phenols, and benzylic alcohols) are suitably protected except for a hydroxyl group on the remaining residue A_4 sugar, which is where an additional sugar is to be attached.

On page 126, please delete the last paragraph (lines 10-26), and insert the following in amended form:

As shown in Figs. 13a and 13b, compound (CXXXIV) (5 mg, 0.00292 mmol) is dissolved in 1 mL methanol and 300 µL DIEA is added. This solution is stirred for 10 minutes and then loaded to a 5mm x 30mm polystyrene column and eluted with methanol/water/1%DIEA (0%, 10%, 20%, 30%, 40%, 50% of 10 mL each). The fractions containing compound (CXXXIV) are combined and concentrated to give a white solid. This white solid is mixed with C-6 amine (III) (10 mg, 0.00582 mmol, purified from silica gel column as free base), azeotroped with toluene 3 times and dissolved in 100 µL DMF. The reaction solution is stirred at 0 °C and DIEA (5 µL, 0.0283 mmol) is added followed by HOBt (2mg, 0.0148mmol) and pyBOP (5 mg, 0.00962 mmol). After 10 minutes, the reaction is directly loaded to a 10mm x 12cm silica gel column and eluted with 30% methanol/$CHCl_3$ to give a crude product. The crude product is purified by reverse-phase HPLC using a PHENOMENEX LUNA C18 column (21.2 x 250mm), 5 micron particle, eluting with a 40 min. linear gradient of 20% acetonitrile/0.1% acetic acid in water to 70% acetonitrile/0.1% acetic acid in water; flow rate of 7 mL/min. and ultraviolet (UV) detection at 285 nm. The fractions containing the product are combined and evaporated to give 2 mg of dimer (CXXXV), 20%. Rf=0.7 (30% $CHCL_3$/MeOH). Mass Spec. $[M+2Na]^+$, 3396.